



THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Efendic et al

Serial No.: 09/754,723

Group Art Unit: 1646

Filed: January 4, 2001

Examiner: To be assigned

Confirmation No. 3358

For: Use Of A Peptide

**AMENDMENT AND RESPONSE TO
NOTICE TO COMPLY WITH SEQUENCE RULES**

Box Sequence
Commissioner for Patents
Washington, DC 20231

Sir:

In response to the Notice to Comply with Sequence Rules dated June 1, 2001,
please amend the above-captioned application as follows:

Please substitute the following paragraph for the same paragraph at page 2, line 25 to page 3,
line 21:

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Glucagon-like peptide-1, also referred to as GLP-1, is a peptide sequence found in the C-terminal portion of mammalian proglucagon. Prior to 1985, no definite biological activity of GLP-1 had been reported. However, in 1985 it was demonstrated that the amide of a fragment of GLP-1, namely GLP-1(1-36)amide, stimulates insulin release from isolated precultured rat pancreatic islets in the presence of glucose in a dose-dependent manner (Schmidt, W.E. et al. *Diabetologia* **28** (1985) 704-7). This finding suggests that GLP-1(1-36)amide and related peptides might be useful in the treatment of type 2 diabetes. Due to its substantially closer sequence homology to glucagon and glucosedeprendent insulinotropic peptide, also referred to as GIP, Schmidt et al. suggested that an even stronger glucagon- and/or GIP-like biological activity could be expected with GLP-1(7-36) than with the intact peptide. In recent years, particular interest has focused on the GLP-1 fragments GLP-1(7-37) and GLP-1(7-36)amide

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and analogues and functional derivatives thereof. The designation GLP-1(1-36) indicates that the peptide fragment in question comprises the amino acid residues from (and including) number 1 to (and including) number 36 when counted from the N-terminal end of the parent peptide, GLP-1. Similarly, the designation GLP-1(7-37) designates that the fragment in question comprises the amino acid residues from (and including) number 7 to (and including) number 37 when counted from the N-terminal end of the parent peptide, GLP-1. The amino acid sequence of GLP-1(7-36)amide and of GLP-1(7-37) is given in formula I (SEQ ID NO:1):

His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-
Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-
Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-X
(I)

which shows GLP-1(7-36)amide when X is NH₂ and GLP-1(7-37) when X is Gly-OH.

Please insert the attached Sequence Listing at the end of the specification following page 15.

T011590 - 320474-000